REMARKS

Claims 1 and 3-34 are pending in the application. Claims 1 and 24 have been amended, and are under examination. Support for the amendments can be found in the originally filed claims and throughout the specification. No new matter has been added.

An Advisory Action was issued on Aug. 25, 2004, indicating that the amended claims filed on Aug. 5, 2004 with the response to the final Office Action dated May 5, 2004, were not found to be allowable. Examiner stated the reasons as follows in the Advisory Action:

"The request for reconsideration has been considered but does NOT place the application in condition for allowance because: the claims as amended do not overcome the prior rejection under 112, 1st paragraph, for enablement. Particularly, the claims recite that the mouse whose endogenous "genes" code for Nav2. This is not enabling because, as stated in prior rejections, the enabling scope of the claims is directed to mice whose genome comprise a homozygous disruption of exon 1 of the endogenous Nav2 gene. Thus, a mouse null mutant mouse whose endogenous genes that code for Nav2 that are inactivated, as claimed, do not fall within the enabled scope of the invention because it implies that there are other genes that may code for endogenous Nav2. Furthermore, the enabled scope of the claimed mice is found to be a homozygous disruption of exon 1. As stated in prior rejections, the state of the art of generating knockout mice teaches that disruption of a different exon may not result in the anticipated phenotype. Thus, the prior rejection of the claims is maintained for reasons of record."

In the above Advisory Action, the meaning of the statement "because it implies that there are other genes that may code for endogenous Nav2" is not quite clear from the context, but Applicant respectfully argue firstly as follows, on the presumption that the Examiner's indication means that "the enabling scope of the claims is directed to mice whose genome comprise a homozygous disruption of exon 1 of the endogenous Nav2 gene" and that mice whose genome comprise a homozygous disruption beyond exon 2 (other than exon 1) are not enabling.

As the Examiner indicates, the possibility that mice whose genome comprise a homozygous disruption beyond exon 2 (other than exon 1) of the endogenous Nav2 gene show a different phenotype from that of mice whose genome comprise a homozygous disruption of exon 1 of the endogenous Nav2 gene is not zero. However, claim 1 relates to a mouse wherein a protein named Nav2 is specifically deleted. In other words, it was found that mice wherein the expression of Nav2 protein is specifically deleted show salt intake behavior similar to that of

wild-type animals under water-sufficient conditions, and show much more intake of hypertonic saline compared with wild-type animals under water-depleted conditions, and thus the invention of claim 1 was completed. Applicant respectfully submits that claim 1 relates to a mouse wherein the expression of Nav2 protein is specifically deleted among mice whose genome comprise a homozygous disruption other than exon 1 of the endogenous Nav2, and not to a mouse expressing Nav2 protein.

As it is well known, as protein is read from the upstream of the encoding gene, when exon 1 being located in the most upstream region is deleted, the genomic function of exons located downstream is also completely deleted. In other words, the absence of exon 1 is considered to be synonymous to the absence of the intended gene itself. Therefore, as the expression of Nav2 protein is specifically deleted in mice whose genome comprises a homozygous disruption of exon 1 of the endogenous Nav2 gene, it is described in claim 1 as: "A null mutant mouse whose endogeous genes that code for Nav2 are inactivated by destruction, deficiency or substitution". As a person of skilled in the art can generate a mouse wherein the expression of Nav2 protein is specifically deleted without undue experimentation, Applicant submits that the invention of claim 1 is enabled.

Next, Applicant respectfully argues on the presumption that "the other gene" in "because it implies that there are other genes that may code for endogenous Nav2" in the above-mentioned Office Action, relates to genes other than the currently targeted Nav2 gene.

Ten types of mammalian sodium channels genes are known up to now, and Nav2 is one of them. However, the amino acid sequence of Nav2 differs significantly from that of the other nine sodium channels gene groups, and there is no gene that could be called to be a second Nav2 gene. Even by supposing that an unknown 11th sodium channel exists, and that this is a second Nav2, Applicant submits that the unknown gene would not the subject of the present claim, as the subject of the present claim is only the targeted Nav2 gene encoded by exon 1 region.

In light of the above amendment, reconsideration and withdrawal of the rejection are respectfully requested.

In light of the amendments and arguments presented, it is believed that the application is in condition for allowance, and notice to that effect is respectfully requested.

Respectfully submitted,

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